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(57) Abstract

A tablet for the local and slow release of herbal medication into the oral cavity of a subject. Also provided is a method of making the tablet and a method of using the tablet. The tablet includes a pharmaceutically effective amount of a herbal medication, a polymeric matrix material such as ethyl cellulose, a release enhancer such as PEG 4000 and a filler such as lactose. The tablet is characterized by long dissolution times of up to 120 minutes.

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LOCAL ORAL HERBAL SLOW RELEASE TABLETS

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to slow release tablets for oral administration and, more particularly, to tablets which permit prolonged interaction between the medication and the buccal and gingival mucosa as well as the hard and soft tissues of the mouth and throat.

Medications are generally administered with a pharmaceutical carrier with specific desired characteristics which can, for example, influence the rate of release of the medication from the carrier. The choice of carrier is thus determined by the desired medical outcome. For example, medications which have local effects in the mouth and throat are often administered in both solid and liquid form, depending upon the desired pharmaceutical effect.

Liquid and semi-liquid dosage forms, such as mouthwashes and toothpaste's are frequently used for oral hygiene, but have the disadvantage of relatively short contact periods with the hard and soft tissues of the mouth and throat. Solid dosage forms, such as troches and lozenges, offer certain advantages for such local administration of oral medications. The terms lozenge and troche are used synonymously for any form of tablet designed to be held in the mouth for slow dissolution and release of medication such that prolonged contact of the medication with the mouth and throat is ensured. The medications administered with troches or lozenges are primarily local anesthetics, antiseptics, astringents or anti-tussives. Lozenges may be made by fusion, a candy molding process or by compression. Troches are usually manufactured by compression, as are most other tablets.

Although currently available troches and lozenges have the advantage of enabling medication to be in prolonged contact with the mouth and throat, such tablets still have a number of disadvantages. First, although troches and lozenges do not dissolve immediately, the rate of release of medication is still relatively rapid, on the order of about 15 minutes for total release. Second, these dosage forms have not been specifically tested with herbal medications, or medications derived from botanical materials. Thus, the efficacy of these dosage forms with herbal medications is unknown. Hereinafter, the term "herbal medication" refers to a medication derived from botanical materials or a biologically active extract of these materials.

The prior art neither taught nor suggested the efficacy of herbal extracts and essential oils using this dosage form.

There is thus a widely recognized need for, and it would be highly advantageous to have, a solid dosage form for oral administration of medication with local effects on the mouth and

throat, which permits release of the medication over a prolonged period of time, which has been specifically tested for use with herbal medications and which permits prolonged contact between the active ingredient of the medication and the hard and soft tissues of the mouth and throat.

SUMMARY OF THE INVENTION

One object of the present invention is to provide a stable tablet for well defined, prolonged and controlled release of a herbal medication in the oral cavity.

A second object is to provide a tablet containing a pharmaceutically effective amount of a herbal medication as the active ingredient, wherein the herbal medication is a herbal extract, essential oil or mixture thereof.

A third object is to provide a method to prepare the tablet for prolonged release of a herbal medication.

According to the present invention there is provided a tablet for prolonged release of a medication, including: (a) a pharmaceutically effective amount of a herbal medication as the medication; (b) a polymeric matrix material; (c) a release enhancer; and (d) a filler. Preferably, the polymeric matrix material is ethyl cellulose. More preferably, the ethyl cellulose is present in an amount of from about 11 percent to about 53 percent, weight per weight. Also preferably, the release enhancer is polyethylene glycol 4000. More preferably, the polyethylene glycol 4000 is present in an amount of from about 8 percent to about 28 percent weight per weight. Preferably, the filler is lactose. More preferably, the lactose is present in an amount of from about 9 percent to about 57 percent weight per weight. Preferably, the herbal medication includes a herbal extract and the tablet further includes fume silica as an absorbing agent for the herbal extract. Preferably, the tablet includes a flavoring agent, a coloring agent or both.

According to another embodiment of the present invention, there is provided a method of releasing a medication in an oral cavity of a subject, including the steps of: (a) placing a tablet in the oral cavity of the subject, the tablet including: (i) a pharmaceutically effective amount of a herbal medication as the medication; (ii) a polymeric matrix material; (iii) a release enhancer; and (iv) a filler; and (b) allowing the tablet to dissolve in the oral cavity of the subject, such that the medication is released.

Hereinafter, the term "subject" is the human to whom the tablet of the present invention is administered.

Hereinafter, the term "herbal medication" can include one or more herbal extracts, one or more essential oils, or a combination of both.

Hereinafter the term "powder" is defined as a dry extract.

Herbal extracts are extracts of plant materials, such as a tincture of botanical materials, which are prepared by contacting botanical material with a solvent [*British Herbal Pharmacopeia*, Peter R. Bradley, ed., British Herbal Medicine Association, 1983; and *British Herbal Compendium*, Peter R. Bradley, ed., British Herbal Medicine Association, 1992]. The solvent can be aqueous or organic, or a combination thereof. Acceptable organic solvents include, but are not limited to, glycerin, propylene glycol or alcohol, or a combination thereof. The most preferred solvents are hydroalcoholic solvents as defined in *British Herbal Pharmacopeia and Compendium*. The botanical material can include, but is not limited to, one or more of the following species: Plantago (*Plantago major*), Hypericum (*Hypericaceae perforatus*), Echinacea (Coneflower) (*Echinaceae* species such as *Echinaceae angustifoliae radix* and *Echinaceae purpurea*), Baptisia, Calendula, Myrrh, Phytolaca, Salvia, Catechu black, Krameria, Tsuga, Rosmarinus, Styrax, Crataegus, Glycerrhiza (*Glycerrhiza glabra*), Angelica, Krameria, Matricaria, Mallow, Sage, Witch Hazel (*Hamamelis vitginiana*), English Oak (*Lobaria*), Burdock (*Arctium Lappa*), Chickweed (*Stellaria*), Sanguinaria Canadensis, Thuja Occidentalis, Balm mint (*Mentha pipereta*), Comfrey (*Symphytum*), and Inula helenium. Propolis is the resinous substance found in beehives. Although strictly speaking Propolis is not a botanical material, extracts of this material are prepared in a substantially similar manner as extracts of the plant materials and are hereinafter included in the term "herbal extract".

An essential oil is a volatile mixture of esters, aldehydes, alcohols, ketones and terpenes, which can be prepared from botanical materials or plant cell biomass from cell culture. Examples of essential oils include, but are not limited to, oil of cinnamon, prepared from the dried bark of the roots of *Cinnamomum zeyloriaceae;* cajeput oil, eucalyptus oil, prepared from the fresh leaves and branches of various species of *Eucalyptus*, such as *E. globulus*; fennel oil, prepared from dried ripe fruit of *Foeniculum vulgare*; geranium oil, prepared from the aerial parts of *Pelargonium* species; girofle oil, lavander oil, prepared from fresh flowering tops of *Lavandula* species such as *Lavandula officinalis*; lemon oil, obtained from the fresh peel of *Citrus limon*; spearmint oil, prepared from the overground parts of fresh flowering *Mentha* species, such as *M. spicata*; peppermint oil (*Mentha Pipereta*), myrte oil, oregano oil, pine oil, rosemary oil, prepared from tops or leafy twigs of *Rosmarinus officinalis*; sarriette oil, thyme oil, prepared from the leaves and flowering tops of *Thymus vulgaris*; tea-tree oil, obtained from the leaves of *Melaleuca olternifolia,* sweet marjoram oil (*Margorana Hortensis*), safflower oil, citronella oil (citronella boil, *Androto Gon Nardus*), garlic oil, and juniper oil (*juniperus*).

BRIEF DESCRIPTION OF THE DRAWINGS

Results of tests performed on tablets of the invention are herein described, by way of example only, with reference to the accompanying drawings, wherein:

FIG. 1 is a graph of the rate of release of the medication contained in the tablets of the present invention of the formulas in Examples 1-4; and

FIG. 2 is a further graph of the rate of release of the medication contained in another embodiment of the tablets of the present invention as shown by a comparison of the tablets of Example 5 and Example 1.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of a solid oral dosage form which enables the slow release of medication in the oral cavity. Specifically, the solid oral dosage form of the present invention enables a prolonged period of contact of the released medication with the mouth and throat, either by slow dissolution or disintegration of the solid dosage form. Furthermore, the solid dosage form is specifically designed to be used with herbal medications, comprising a combination of a herbal extract and essential oil. The solid dosage form is stable and the slow release is well defined and controlled. The use of a herbal extract and essential oil in this type of formulation has not been taught in the prior art. It should be noted that the use of natural herbal extracts and essential oils vastly differs from the use of synthetic medication, even containing the same active ingredient. Plant extracts are made up of numerous components and different sources of the same extracts are not necessarily the same.

Although the following description will refer to the solid dosage form as a "tablet" for the sake of clarity, it should be understood that the present invention is not restricted to any one type of tablet, but could also be in the form of troches or lozenges, for example.

Formulations of Slow Release Tablets

The slow release tablets of the present invention include the following ingredients: the herbal medication itself, a polymeric matrix material, a release enhancer and a filler.

The choice of a particular polymeric matrix material, as well as the amount which is used, has a strong influence on the rate of release of medication from the tablets of the present invention. Examples of polymers for matrix formation include both hydrophobic and hydrophilic polymers. Examples of hydrophobic polymers include, but are not limited to, ethyl

cellulose and other cellulose derivatives, fats such as glycerol palmito-stereat, beeswax, glycowax, castorwax, carnaubawax, glycerol monostereate or stearyl alcohol, hydrophobic polyacrylamide derivatives and hydrophobic methacrylic acid derivatives, as well as mixtures of these polymers. Hydrophilic polymers include, but are not limited to, hydrophilic cellulose derivatives such as methyl cellulose, hydroxypropylmethyl cellulose, hydroxyethylcellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium carboxymethylcellulose and hydroxyethyl methylcellulose, as well as mixtures of these polymers. Furthermore, any mixture of one or more hydrophobic polymer and one or more hydrophilic polymer could optionally be used.

Ethyl cellulose is particularly preferred as the polymeric matrix material for the tablets of the present invention, and is preferably present in an amount of from about 11 to about 53 percent, weight per weight.

Examples of release enhancers which modify the rate at which medication is released from the polymeric matrix material include, but are not limited to, glycerol and polyethylene glycols (PEG) of different molecular weights, e.g. PEG 300, PEG 400, PEG 1000, PEG 4000, PEG 6000, PEG 10,000 and others. PEG 4000 is the preferred release enhancer because it causes the polymeric matrix material to dissolve slowly in aqueous solutions. PEG 4000 is preferably present in an amount of from about 8 to about 28 percent, weight per weight.

Examples of pharmaceutically acceptable fillers include lactose, sucrose, mannitol and others. Lactose is the preferred filler and is preferably present in an amount of from about 9 to about 57 percent, weight per weight. Optional ingredients include coloring and flavoring agents which are well known in the art.

Preparation of the tablets of the present invention requires the addition of a wetting agent at one point in the procedure. The wetting agent is preferably a solution of water and alcohol. However, it should be noted that one ingredient in the tablets of the present invention can be a herbal extract, which is itself a liquid. The addition of the herbal extract to the tablet presents a challenge, since large amounts of liquid are not well incorporated into tablets, which are dry solids. This problem is solved in one of two ways.

The first solution is simply to use the herbal extract itself as the wetting agent. Since, as noted previously, herbal extracts are prepared by contacting botanical materials with a solvent which is preferably a mixture of alcohol and water, the herbal extract contains the same liquid ingredients as the wetting agent. Therefore, the herbal extract is an ideal replacement for the standard wetting agent.

However, in some instances, it is desirable to add such large quantities of herbal extract that even substituting the extract for the wetting agent is not sufficient. This problem is solved by first absorbing some or all of the herbal extract onto fume silica, which is an absorbing agent with a large absorbent surface area. The combination of the extract and the fume silica can be added to the tablet without destroying the integrity of the tablet itself. Fume silica is commercially available from Rhone-Poulenc, France as "Tixosil", for example.

The essential oil and herbal extract are preferably present in a combined amount of from about 0.5 to about 40 percent, weight per weight and most preferably of from about 4 to about 25 percent, weight per weight in the tablet.

The ratio of essential oil to herbal extract in the tablet is in the range of from about 1:4 to about 1:30.

A number of examples of tablets of the present invention are given below for purposes of illustration only and are not intended to be limiting. Furthermore, for the purposes of evaluation only and unless otherwise detailed, the herbal medication used in the methods detailed below was natural xantines from freeze-dried ripe seeds of *Coffea rubiaceae*, added in the form of coarsely ground powder, hereinafter referred to as "coffee powder", and an essential oil. The essential oil used was Eucalypti oil, Cinnamon oil or Tea tree oil, although other oils could also be used, alone or in combination.

The tablets of the present invention were evaluated by using the following methods. Two separate tests were performed, a dissolution and release test in a standard rotating basket assembly, and a release test in the oral cavity of a subject.

The dissolution test was performed in accordance with the USP (United States Pharmacopeia). The speed of rotation of the basket was 150 revolutions per minute. The dissolution medium was 0.9% NaCl solution in purified water. The basket was a cylindrical vessel with a flat bottom capable of holding 1000 ml of dissolution medium. For the release test in the standard assembly, results are presented as the percentage of herbal medication released over time.

For the release test in the oral cavity, five separate tests were performed on five separate human subjects. Each subject held the tablet in the mouth and timed how long the tablet took to completely dissolve or disintegrate. Thus, this was an *in vivo* test of the performance of the tablets of the present invention. Furthermore, this test is substantially identical to the actual method of use of the tablets of the present invention.

The formulation and method of production of each tablet is given below as a separate, illustrative example.

Example 1

The tablet of Example 1 had the following ingredients, as given in the table below.

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	20.0
PEG 4000	25.0
Lactose	25.0
Coffee Powder	28.0
Eucalypti oil	2.0

The method of preparation of this tablet formulation was as follows. A thick dough was obtained by massing about 5 g of PEG 4000 with about 6.0 ml of ethanol (absolute). A powdered mixture of about 5 g of lactose and 5.6 g of coffee powder was added to the thick dough. About 1.5 ml of ethanol was then added to finish the massing of the dough. The dough was then pressed through a 1.6 mm screen of an Eureka granulation machine to form a granulation. The granulation was dried in an oven at about 53 °C for 1.5 hours.

After cooling, the mixture was ground with a hand-held mortar and pestle. Eucalypti oil was added to the ground mixture by dispersion to form the final granulation. This granulation was then compressed into tablets in a tablet press. The tablet compression was about 10 Torr, for a tablet of about 1 g weight, 10 mm diameter and 4 mm thickness.

The tablet was tested by using the diand release tests described below. After 65 minutes in the dissolution test, the percentage of herbal medication released was 32%. During the oral release test, the tablet completely dissolved after about 45-50 minutes.

Example 2:

The tablet of Example 2 had the following ingredients, as given in the table below.

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	30.0
PEG 4000	20.0
Lactose	20.0
Coffee Powder	28.0
Eucalypti oil	2.0

The tablets were prepared as for Example 1 above, except that the proportions of the ingredients were changed. After 65 minutes, the percentage of herbal medication released was about 24.7%. The tablets required about 65-70 minutes in the oral cavity to completely dissolve.

Example 3

The tablet of Example 3 had the following ingredients, as given in the table below.

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	50.0
PEG 4000	10.0
Lactose	10.0
Coffee Powder	28.0
Eucalypti oil	2.0

The tablets were prepared as for Example 1 above, except that the proportions of the ingredients were changed. After 65 minutes, the percentage of herbal medication released was about 18.6%. The tablets required about 120 minutes in the oral cavity to completely dissolve.

Example 4

The tablet of Example 4 had the following ingredients, as given in the table below.

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	11.5
PEG 4000	8.0
Lactose	54.5
Coffee Powder	24.0
Eucalypti oil	2.0

The tablets were prepared as for Example 1 above, except that the proportions of the ingredients were changed. After 65 minutes, the release profile was about 68.6%. The tablets required about 10-15 minutes in the oral cavity to completely dissolve.

The results of the tests performed in the standard rotating basket assembly for the tablets of Examples 1-4 are given in Figure 1. Figure 1 shows the results of the release test, with the release profile given as a percentage over time. The diamonds indicate results obtained for the tablet of Example 1. Similarly, squares indicate tablets of Example 2, triangles tablets of Example 3 and crosses tablets of Example 4. Clearly, tablets of Example 4 dissolved the most quickly and tablets of Example 3 dissolved the most slowly.

Table 1 shows the results for the oral release test, conducted on the tablets of Examples 1-4. Again, tablets of Example 4 released the herbal medication the most quickly, and those of Example 3 released the medication the most slowly. Thus, the results of the *in vitro* and *in vivo* tests match in terms of the relative table dissolution rates.

Table 1. Results of Oral Release Test

Formula	Time for Complete Tablet Disintegration *In Vivo*
Example 4	10-15 minutes
Example 1	45-50 minutes
Example 2	65-70 minutes
Example 3	120 minutes

Example 5

The tablet of Example 5 had the following ingredients, as given in the table below.

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	20.0
PEG 4000	25.0
Lactose	15.0
Propolis Powder	15.0
Myrrh Powder	15.0
Cinnamon oil	2.0

The tablets were prepared as for Example 1 above, except that the herbal medication was a combination of Myrrh and Propolis powders, and of Cinnamon oil, rather than ground coffee and Eucalypti oil. The results of a comparison of the release rate to tablets of Example 1 is given in Figure 2. As can be seen from Figure 2, tablets of Example 5 dissolved much more slowly than tablets of Example 1.

Other Formulas for Slow Release Tablets

Other examples of suitable formulas for slow release tablets according to the present invention are given below.

Example 6

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	15.7
PEG 4000	19.6
Lactose	27.5
Myrrh	5.0
Propolis	10.73
Plantago	0.21
Hypericum	0.27
Coneflower	0.20
Menthe oil	5.0
Tixosil 43	15.6
Sodium saccharin	0.19

It should be noted that three of the ingredients, Plantago, Hypericum and Coneflower, are liquid extracts (tinctures) which are present in a total amount of 39% volume per total weight of the tablet.

Tablets of Example 6 were prepared as follows. First, the liquid extracts were mixed together. Next, sodium saccharin was mixed with the liquid extracts. This mixture was added to powdered PEG 4000 to form a second mixture. An ethyl cellulose mixture was prepared by mixing ethyl cellulose with 3.5 ml of ethanol. The second mixture and the ethyl cellulose mixture were then mixed well in a mortar. Lactose, Myrrh and Propolis were then added to the mixture in the mortar to form a dough. Tixosil 43 (fume silica) was then added to the dough to form the final dough. The final dough was then pressed through a 1.6 mm screen of an Eureka granulation machine to form a granulation. The granulation was dried in an oven at about 53 °C for 1.5 hours.

After cooling, the mixture was ground with a hand-held mortar and pestle. Menthe oil was added to the ground mixture by dispersion to form the final granulation. This granulation was then compressed into tablets in a tablet press. The tablet compression was about 10 Torr, for a tablet of about 1 g weight, 10 mm diameter and 4 mm thickness.

Example 7

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	15.7
PEG 4000	19.6
Lactose	27.5
Myrrh	5.0
Propolis	10.73
Plantago	0.21
Hypericum	0.27
Coneflower	0.20
Menthe oil	2.5
Thyme oil	2.5
Tixosil 43	15.6
Sodium saccharin	0.19

It should be noted that as in Example 6, three of the ingredients, Plantago, Hypericum and Coneflower, are liquid extracts (tinctures).

Tablets of Example 7 were prepared as for tablets of Example 6, except that both Menthe oil and Thyme oil were added to the ground mixture by dispersion to form the final granulation.

Example 8

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	15.7
PEG 4000	19.6
Lactose	27.5
Myrrh	5.0
Propolis	10.73
Plantago	0.21
Hypericum	0.27
Coneflower	0.20
Menthe oil	3.0
Cinnamon oil	2.0
Tixosil 43	15.6
Sodium saccharin	0.19

It should be noted that as in Example 6, three of the ingredients, Plantago, Hypericum and Coneflower, are liquid extracts (tinctures).

Tablets of Example 8 were prepared as for tablets of Example 6, except that both Menthe oil and Cinnamon oil were added to the ground mixture by dispersion to form the final granulation.

Example 9

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	15.7
PEG 4000	19.6
Lactose	27.5
Myrrh	1.0
Propolis	14.73
Plantago	0.21
Hypericum	0.27
Coneflower	0.20
Menthe oil	3.0
Cinnamon oil	2.0
Tixosil 43	15.6
Sodium saccharin	0.19

It should be noted that as in Example 6, three of the ingredients, Plantago, Hypericum and Coneflower, are liquid extracts (tinctures).

Tablets of Example 9 were prepared as for tablets of Example 8.

Example 10

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	15.7
PEG 4000	19.6
Lactose	27.5
Myrrh	1.0
Propolis	14.73
Plantago	0.21
Hypericum	0.27
Coneflower	0.20
Thyme oil	3.0
Cinnamon oil	2.0
Tixosil 43	15.6
Sodium saccharin	0.19

It should be noted that as in Example 6, three of the ingredients, Plantago, Hypericum and Coneflower, are liquid extracts (tinctures).

Tablets of Example 10 were prepared as for tablets of Example 6, except that both Thyme oil and Cinnamon oil, instead of Menthe oil, were added to the ground mixture by dispersion to form the final granulation.

Example 11

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	11.27
PEG 90 (PEG 4000)	14.06
Lactose	25.00
Plantein extract	8.44
Hypericum Perforatum extract	8.44
Coneflower (Echinacea purpurea) extract	8.44
Sodium Saccharin	0.14
Myrrh (powder)	1.43
Propolis extract	7.18
Hydrated silica (Tixosil 43)	11.48
Benecoat BMI-60	0.72
Thyme (Lemon Thyme) oil	1.70
Mentha (Peppermint) oil	1.70

The components were weighed out. Ethyl cellulose and PEG 90 were transferred to the mixer and mixed for ten minutes. Plantain, Hypericum and coneflower extracts were mixed and sodium saccharin was then added. This mixture was added to the ethyl cellulose mixture and ethyl alcohol was added (approximately 13-14% v/w of the total weight) to give the right constituency of the powdered mixture. BMI-60 was mixed with powdered propolis and myrrh and this was added to the alcohol containing mixture. Lactose was added and massed and then Tixosil 43 was added to obtain a dough.

The dough was pressed through a 1.6mm screen. The obtained granulate was dried at 55-58°C for three hours. The prepared granulate was then cooled down to room temperature. The oils that have been mixed were dispersed on the surface of the granulate. The resulting dry granulate was then pressed through a 1.6mm screen.

Example 12

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	10.0
PEG-75	20.0
Lactose	55.7
Lemon base powder	2.5
Wild Indigo Extract	3.00
Coneflower Extract	2.00
Myrrh Extract	2.00
Propolis Extract	2.00
Sage Extract	2.00
Thyme oil	0.60
Sodium Saccharin	0.20
Ethanol	

The tablets of Example 12 was prepared as in Example 11. The extracts used were Wild Indigo, Coneflower, Myrrh, Propolis and Sage, lemon base powder was used and the essential oil used was Thyme oil.

Example 13

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	11.3
PEG 90 (PEG 4000)	14.1
Lactose	43.0
Coneflower extract	8.00
Propolis Wax (powder)	3.00
Myrrh (Commiphora Myrrha) resin	1.50
Hydrated silica (Tixosil 43)	15.95
Benecoat BMI-60	1.00
Cinnamomum Zeylanicum oil	1.00
Thyme (Lemon Thyme oil)	1.00
Sodium Saccharin	0.14

Tablets of Example 13 were prepared as for Example 11, except the extracts used were Coneflower, the dry extracts were Propolis and Myrrh and the essential oils were Cinnamomum Zeylanicum oil and Thyme (Lemon Thyme oil).

Example 14

Tablet Ingredients	Amount (% weight per weight)
Ethyl Cellulose	11.30
PEG 90 (PEG 4000)	14.11
Lactose	25.00
Calendula extract	8.00
Poke Root extract	8.00
Coneflower extract	8.00
Propolis (powder)	7.00
Hydrated silica (Tixosil 43)	16.45
Thyme oil	2.00
Sodium Saccharin	0.14

The components were weighed out. Ethyl cellulose and PEG 90 were transferred to the mixer and mixed for ten minutes. Calendula, Poke Root and coneflower extracts were mixed and sodium saccharin was then added. This mixture was added to the ethyl cellulose mixture and ethyl alcohol was added (approximately 13-14% v/w of the total weight) to give the right constituency of the powdered mixture. Powdered propolis was added to the alcohol containing mixture. Lactose was added and massed and then Tixosil 43 was added to obtain a dough.

The dough was pressed through a 1.6mm screen. The obtained granulate was dried at 55-58°C for three hours. The prepared granulate was then cooled down to room temperature. The oils that have been mixed were dispersed on the surface of the granulate. The resulting dry granulate was then pressed through a 1.6mm screen.

It will be appreciated that the above descriptions are intended only to serve as examples, and that many other embodiments are possible within the spirit and the scope of the present invention.

WHAT IS CLAIMED IS:

1. A tablet for prolonged release of a medication, comprising:

(a) a pharmaceutically effective amount of a herbal medication as the medication;

(b) a polymeric matrix material;

(c) a release enhancer; and

(d) a filler.

2. The tablet of claim 1, wherein said polymeric matrix material is ethyl cellulose.

3. The tablet of claim 2, wherein said ethyl cellulose is present in an amount of from about 11 percent to about 53 percent, weight per weight.

4. The tablet of claim 1, wherein said release enhancer is polyethylene glycol 4000.

5. The tablet of claim 4, wherein said polyethylene glycol 4000 is present in an amount of from about 8 percent to about 28 percent weight per weight.

6. The tablet of claim 1, wherein said filler is lactose.

7. The tablet of claim 6, wherein said lactose is present in an amount of from about 9 percent to about 57 percent weight per weight.

8. The tablet of claim 1, wherein said herbal medication includes a herbal extract, the tablet further comprising fume silica as an absorbing agent for said herbal extract.

9. The tablet of claim 1, further comprising a coloring agent.

10. The tablet of claim 1, further comprising a flavoring agent.

11. A method of releasing a medication in an oral cavity of a subject, comprising the steps of:

(a) placing a tablet in the oral cavity of the subject, the tablet including:

(i) a pharmaceutically effective amount of a herbal medication as the medication;

(ii) a polymeric matrix material;

(iii) a release enhancer; and

(iv) a filler;

and

(b) allowing said tablet to dissolve in the oral cavity of the subject, such that the medication is released.

12. The method of claim 11, wherein said polymeric matrix material is ethyl cellulose.

13. The method of claim 12, wherein said ethyl cellulose is present in an amount of from about 11 percent to about 53 percent, weight per weight.

14. The method of claim 11, wherein said release enhancer is polyethylene glycol 4000.

15. The method of claim 14, wherein said polyethylene glycol 4000 is present in an amount of from about 8 percent to about 28 percent weight per weight.

16. The method of claim 11, wherein said filler is lactose.

17. The method of claim 16, wherein said lactose is present in an amount of from about 9 percent to about 57 percent weight per weight.

18. The method of claim 11, wherein the herbal medication includes a herbal extract, said tablet further including fume silica as an absorbing agent for said herbal extract.

19. The method of claim 11, wherein said tablet further includes a coloring agent.

20. The method of claim 11, wherein said tablet further includes a flavoring agent.

21. The tablet of claim 1, wherein said herbal medication is at least one essential oil or a mixture of essential oils.

22. The tablet of claim 1, wherein said herbal medication is a mixture of at least one essential oil and at least one herbal extract.

23. The tablet of claim 8, wherein said herbal extract includes Plantago (*Plantago major*), Hypericum (*Hypericaceae perforatus*), Echinacea (Coneflower) (*Echinaceae* species such as *Echinaceae angustifoliae radix* and *Echinaceae purpurea*), Baptisia, Calendula, Myrrh, Phytolaca, Salvia, Catechu black, Krameria, Tsuga, Rosmarinus, Styrax, Crataegus, Glycerrhiza (*Glycerrhiza glabra*), Angelica, Krameria, Matricaria, Mallow, Sage, Witch Hazel (*Hamamelis vitginiana*), English Oak (Lobaria), Burdock (Arctium Lappa), Chickweed (Stellaria), Sanguinaria Canadensis, Thuja Occidentalis, Balm mint (Mentha pipereta), Comfrey (Symphytum), Propolis and Inula helenium.

24. The tablet of claim 21, wherein said essential oil includes cinnamon oil, cajeput oil, eucalyptus oil, fennel oil, geranium oil, girofle oil, lavender oil, lemon oil, spearmint oil, peppermint oil (*Mentha Pipereta*), myrte oil, pine oil, rosemary oil, sarriette oil, thyme oil, tea-tree oil, sweet marjoram oil (*Margorana Hortensis*), safflower oil, citronella oil, garlic oil, juniper oil (*juniperus*) and oregano oil.

25. The tablet of claim 22, wherein said mixture of said at least one essential oil and said at least one herbal extract are present in an amount of from about 4 percent to about 25 per cent weight per weight.

26. The tablet of claim 22, wherein the ratio of said at least one essential oil to said at least one herbal extract is from about 1 to 4 to about 1 to 30.

27. The tablet of claim 22 wherein said at least one herbal extract is propolis and myrrh and said at least one essential oil is cinnamon oil.

28. The tablet of claim 22 wherein said at least one herbal extract is myrrh, propolis, plantago, hypericum and coneflower and said at least one essential oil is menthe oil.

29. The tablet of claim 22 wherein said at least one herbal extract is myrrh, propolis, plantago, hypericum and coneflower and said at least one essential oil is menthe oil and thyme oil.

30. The tablet of claim 22 wherein said at least one herbal extract is myrrh, propolis, plantago, hypericum and coneflower and said at least one essential oil is menthe oil and cinnamon oil.

31. The tablet of claim 22 wherein said at least one herbal extract is plantago, hypericum, coneflower, myrrh and propolis and said at least one essential oil is thyme oil and mentha oil.

32. The tablet of claim 22 wherein said at least one herbal extract is lemon, wild indigo, coneflower, myrrh, propolis and sage and said at least one essential oil is thyme oil.

33. The tablet of claim 22 wherein said at least one herbal extract is coneflower, propolis and myrrh and said at least one essential oil is thyme oil and cinnamon oil.

34. The tablet of claim 22 wherein said at least one herbal extract is calendula, poke root, coneflower and propolis and said at least one essential oil is thyme oil.

35. A method of preparation of a tablet for prolonged release of a medication, comprising:
the steps of:

(a) making the dough and forming a granulate;

(b) dispersing mixture of oils on the surface of said granulate; and

(c) pressing said granulate to form a tablet.

36. A tablet for prolonged release of a medication, comprising:

(a) a pharmaceutically effective amount of a medication consisting essentially of an herbal medication;

(b) a polymeric matrix material;

(c) a release enhancer; and

(d) a filler.

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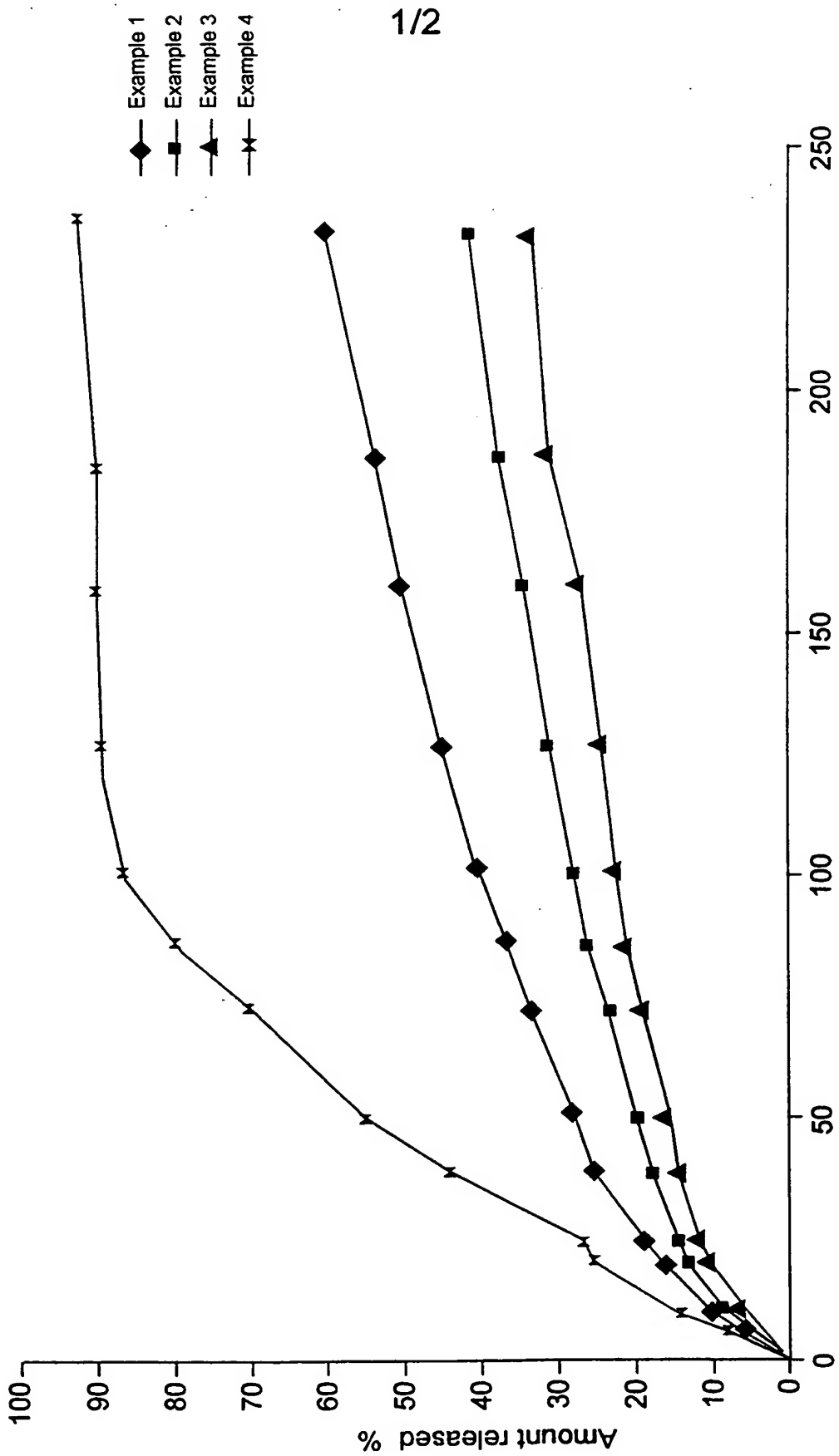

Fig. 1 Release rates from tablets

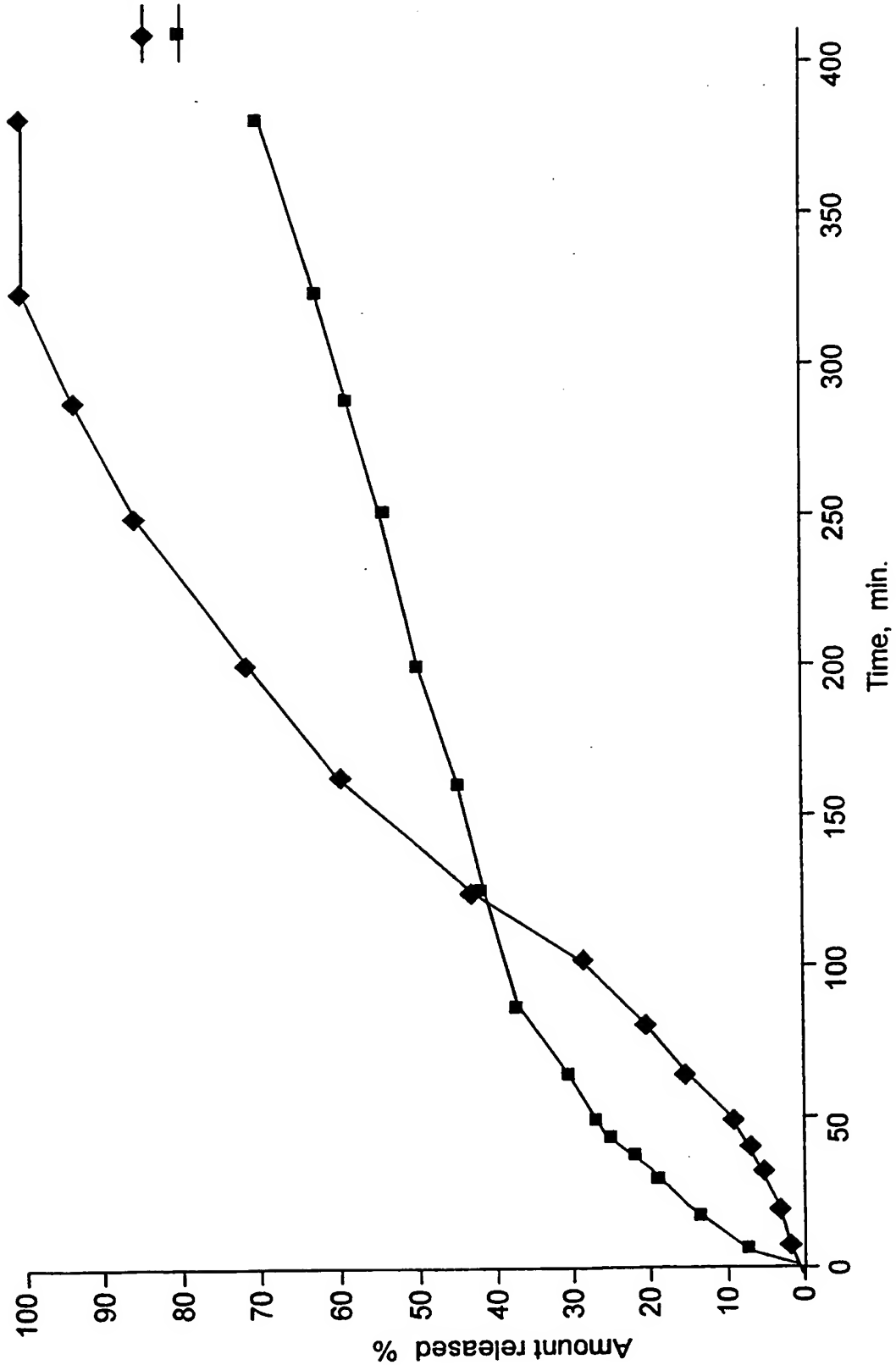

Fig. 2 Comparison of example 1 and 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/16477

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 9/20, 9/22, 9/26
US CL :424/435, 464, 465, 468, 469, 470

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/435, 464, 465, 468, 469, 470

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,292,299 A (SUZUKI et al) 29 September 1981, see column 2, line 43 through column 3, line 29, column 5, lines 6-57, Table 1, claims 1-9.	1-22, 35 and 36
Y	US 4,039,653 A (DeFONEY et al) 02 August 1977, see entire document, especially columns 7-9.	1-22, 35 and 36

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
19 OCTOBER 1998	29 OCT 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JAMES M. SPEAR for Telephone No. (703) 308-1235

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